REMARKS

Claims 1-16 are pending in the subject application. Applicant confirms the election with traverse of group I claims 1-16 in response to the restriction requirement and cancel claims 17-36 without prejudice or disclaimer. Applicant confirms the election with traverse of naproxen as a species selection. The amendment to claim 12 is made merely to correct a typographical error; no new matter is added to the claims.

1. The Amended Claims are patentable over the Art Cited Under 35 U.S.C. § 103(a).

1.1. The Rejection of Claims 1-16 under 35 U.S.C. § 103(a) over WO 99/44623

Claims 1-16 stand rejected under 35 U.S.C. § 103(a) as being unpatentably obvious over WO 99/44623 ("WO") (abstract; page 4, lines 3-15; page 6, lines 6-20). Examiner asserts that WO teaches that hops and naproxen can be in the same composition, and that it would have been obvious to select them from a list in WO list because they are both noted to be used in a single composition to treat inflammation. Applicant respectfully disagrees that the combination of components of the present invention would have been obvious to one skilled in the art.

In the present invention, the addition of hops extracts to naproxen or other non-steroidal anti-inflammatory drugs (NSAIDs) not only yields an enhanced anti-inflammatory effect over NSAIDs alone, but the combination also reduces the gastropathy of the NSAID. WO only suggests that the combination a NSAID with hops that have been treated to specifically produce isovaleric or isovaleramide may decrease inflammation and muscle tone associated with muscle pain.

1.1.1. WO suggests isovaleric acid and NSAIDs reduce muscle tone and inflammation

WO recites "there has been provided a use of an extract of . . . hops in combination with at least one non-steroidal anti-inflammatory compound . . . for use in a method of treating acute muscular aches, strains, and sprains," (page 4, lines 3-15). The key characteristic WO emphasizes of the hops extract is that it is "hydrolyzed *in vivo* to yield isovaleric acid or isovaleramide (page 26, claim 15), which is purported to decrease muscle tone associated with muscle pain: "the dosages of the muscle-tone decreasing agents and the NSAID compounds described herein . . ." (page 18, lines 24-25).

WO does not discuss experiments involving hops, but suggests that results of experiments involving valerian extract would produce similar results if practiced with hops. In the description regarding Valerian extracts which WO uses as an alternative for hops, WO recites "Valerian extracts and valerian-related compounds can be administered in combination with at least one NSAID compound, such as ibuprofen, *in vivo*, to reduce acute muscle pain by decreasing muscle tone and inflammation." (page 6, lines 28-30). Throughout the application, WO suggests that the expected results from the combination of isovaleric acid or isovaleramide yielded from hops extract with a NSAID such as naproxen would be an increased anti-inflammatory response and decreased muscle tone to increase relief of muscle pain.

1.1.2. The present invention teaches hops extracts with NSAIDs to reduce NSAIDs-gastropathic side effects

The combination of hops extracts with naproxen for the use in the present invention is not obvious over WO, because unexpected results were obtained. The current invention's combination of hops extracts with naproxen not only yields a greater anti-inflammatory response than hops extracts or NSAIDs alone, but also the hops extracts "prevent or attenuate gastropathy, and particularly but not exclusively that caused by non-steroidal anti-inflammatory drugs." (para 2; lines 5-8).

NSAIDs inhibit the production of cyclooxygenase (COX) which catalyzes the rate limiting step in the production of prostraglandins (PGs) which cause inflammatory responses. COXs are of two types: COX-1, which affects PGs that maintain physiological functions such as regulation of gastric mucosa, renal blood flow and platelet aggregation, and COX-2 which affects PGs that mainly increase inflammation. NSAIDs alone inhibit both COX-1 and COX-2, which leads to gastric irritation and potentially gastric bleeding and/or kidney damage. (para. 5-7; para.15, lines 1-2). The present invention has found "that chemically induced ulceration, produced by analgesic and/or anti-inflammatory drugs such as ibuprofen, aspirin and indomethacin, or other chemical agents, is significantly reduced when these drugs are administered in combination with hop derivatives." (para. 42). A reduction in ulceration from a hops extract and NSAID combination is unexpected from the teachings of WO.

When hops extracts are combined with NSAIDs, a decreased inhibition of PGs in gastric mucosal cells is found compared to the use of NSAIDs alone. (Examples 5 and 6). While also yielding a reduction in inflammation, the addition of hops extracts to NSAIDs in the present invention yields the unexpected result of decreased gastric ulceration caused by NSAIDs because the compounds leading to formation of gastric mucosa are inhibited less. The effect of hops derivatives with naproxen would be similar to the results obtained with ibuprofen or aspirin in examples 5 and 6, because, as is known to persons of skill in the art, NSAIDs work by inhibiting COX-1, which catalyzes the reactions for PGs which maintain physiological functions. Decreased inhibition of PGs that maintain physiological functions would be directly related to the inhibition by hops of COX-1, whether the inhibition of COX-1 was caused by ibuprofen, aspirin, naproxen, or any other NSAID. Because hops derivatives prevent the inhibition of COX-1, a decrease in PGs that maintain physiological function is also prevented, regardless of the particular NSAID targeting COX-I.

1.1.3. The present invention teaches combinations of compounds not obvious over WO

The present invention further is not obvious over WO because WO only teaches combinations of NSAIDs with hops extracts that hydrolyze *in vivo* to produce isovaleric acid or isovaleramide, whereas the present invention teaches combinations of NSAIDs with hop extracts or with extracts containing compounds of the Supragenus structure (claim 3) or of the Genus A or B structure (claims 4-5), all of which extracts that do not necessarily hydrolyze to yield isovaleric acid or isovaleramide. Further, WO does not teach or suggest hops extracts containing compounds having the formulas of Supragenus (claim 3), Genus A or B (claims 4 – 5).

Applicants respectfully submit that the foregoing amendments and remarks have fully addressed the Examiner's rejection under 35 U.S.C. § 103 and, therefore, request its removal.

1.2. The Rejection of Claims 1-16 Based on JP 406312924 (abstract) or JP 04202138 (abstract)

Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP 406312924 (abstract) or JP 04202138 (abstract) taken with Sunshine et al. (US patent No. 4780463) or CA 2175091 (abstract).

Examiner asserts that JP 406312924 (abstract) or JP 04202138 (abstract) both teach hops extracts used to treat inflammation. Examiner asserts that both Sunshine et al. (US patent No. 4780463) and CA 2175091 (abstract) teach the use of naproxen to treat inflammation.

As described above, the present invention teaches the use of hops extract with naproxen or other NSAIDs to reduce the physiological problems, such as gastropathy, caused by NSAIDs' inhibition of COX-1. This use of hops is not used to treat inflammation, but rather to extinguish or ameliorate the gastropathic side effects of naproxen or other NSAIDs. The results of the present invention which are discussed above in section 1.1, are not obvious over the cited prior art, which only suggest a combination of hops with NSAIDs reduces inflammation, but not that the combination reduces the side effects caused by NSAIDs' inhibition of COX-1.

For the foregoing reasons, applicants aver that the claimed invention is not obvious over the cited prior art. Accordingly, it is respectfully requested that the rejection of claims 1-16 under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

Accordingly, it is respectfully requested that the rejection of claims 1-8 under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

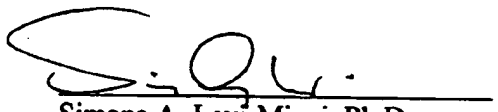
CONCLUSION

It is submitted that the amended claims are patentable over the teachings of the prior art relied upon by the Examiner. Accordingly, favorable reconsideration of the claims is requested in light of the preceding amendments and remarks. Allowance of the claims is courteously solicited.

If there are any outstanding issues that might be resolved by an interview or an Examiner's amendment, the Examiner is requested to call Applicant's attorney at the telephone number shown below.

Pursuant to 37 C.F.R. § 1.136(a)(2), the Examiner is authorized to charge any fee under 37 C.F.R. § 1.17 applicable in this instant, as well as in future communications, to Deposit Account 50-1133. Furthermore, such authorization should be treated in any concurrent or future reply requiring a petition for an extension of time under Section 1.136 for its timely submission, as constructively incorporating a petition for extension of time for the appropriate length of time pursuant 37 C.F.R. § 1.136(a)(3) regardless of whether a separate petition is included.

Respectfully submitted,
McDERMOTT WILL & EMERY LLP



Simona A. Levi-Minzi, Ph.D.
Registration No. 43,750
Attorney for Applicants

McDermott Will & Emery LLP
201 South Biscayne Boulevard
Suite 2200
Miami, Florida 33131
Telephone: 305.347.6515
Facsimile: 305.347.6500
E-Mail: SLEVI@MWE.COM

Date: February 14, 2006